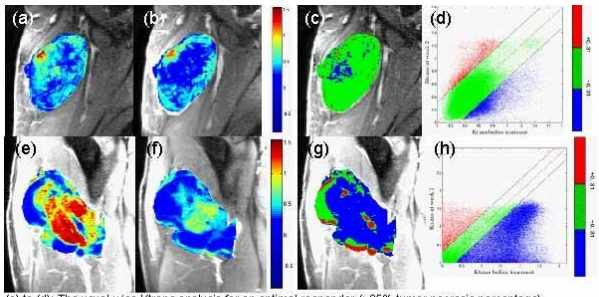
patients with high-risk extremity soft tissue sarcoma. A two-tier registration was used to align the tumor VOI within each dynamic frame at TP1 and align the volumes at TP2 to the volumes at TP1. After registration, the voxel-wise transfer constant K^{trans} within a VOI covering the whole tumor normalized to a reference region of normal tissue area closed to the tumor was calculated. The responder threshold was determined by linear regression via evaluating the 95% confidence interval [-T, T] in the residuals from the reference region. The difference of the voxel-wise ΔK^{trans} within the tumor between TP1 and TP2 was calculated. Three classes of voxels within the tumor VOI were determined: voxels having ΔK^{trans} value exceed threshold T were designated in red, below -T were designated in blue, and otherwise designated in green indicating no significant change. The volume fractions with respect to three sub-volumes of the tumor VOI were computed as F_+ (red voxels), F_-(blue voxels) and F_0 (green voxels).

Results: The histopathology at the time of surgery confirmed that 3 patients were optimal responders to preoperative treatment (≥95% pathologic tumor necrosis percentage) and 9 patients were sub-optimal responders (<95% necrosis percentage).F_0, ΔK^{trans} and F_- had significantly positive, positive and negative correlations with necrosis percentage ($p < 0.05$), respectively. The change of tumor size had no correlation with necrosis percentage.



(a) to (d): The voxel-wise Ktrans analysis for an optimal-responder (>95% tumor necrosis percentage). (a) Voxel-wise Ktrans colormap at TP1, (b)Voxel-wise Ktrans colormap at TP2, (c) Voxel-wise Ktrans map of three classes of voxels depicted as red (increased Ktrans), green (no change beyond 95% confidence intervals), and blue (decreased ktrans); (d) Scatter plots of three classes of voxels.

(e) to (h): The voxel-wise Ktrans analysis for a sub-optimal responder (30% tumor necrosis percentage). (e)Voxel-wise Ktrans colormap at TP1; (f)Voxel-wise Ktrans colormap at TP2; (g)Voxel-wise Ktrans map of three classes of voxels depicted as red (increased Ktrans), green (no change beyond 95% confidence intervals), and blue (decreased ktrans); (h)Scatter plots of three classes of voxels.

The areas under the curve (AUC) values and P-values of the ROC analysis.

Biomarkers	AUC	P
F_+	0.556	0.782
F_0	0.852	0.079
F_-	0.889	0.052
$\Delta size$	0.556	0.782
mean ΔK^{trans}	0.815	0.116

Conclusion: The results suggest that F_0 and $F_-$are more sensitive to early therapy response compared, which could provide the early prediction of treatment outcome while retain spatial localization of heterogeneous response to treatment in sarcoma.

EP-1851

Quantitative assessment of glucose metabolic rate within NSCLC histologies using dynamic 18F-FDG PET

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Purpose or Objective: Biological behavior differs between histologies of non-small cell lung cancer (NSCLC). Tumour biology and glucose metabolism influence radiosensitivity. The first goal of this study is to calculate glucose metabolic rate constants k1 (glucose transporter (GLUT) influx), k2 (GLUT efflux), k3 (hexokinase phosphorylation) and blood volume (VB) in adeno- versus squamous cell NSCLC using dynamic 18FDG PET. Heterogeneity of these parameters will be assessed within different tumour regions. This will improve understanding tumour biology and potentially form the basis for dose modifications in radiotherapy.
Besides 18FDG PET as a tool indicating radioresistant tumour areas, PET may be used for tumour delineation in radiotherapy planning. Manual tumor delineation of stage III NSCLC for radiotherapy planning takes a lot of effort. The second objective of this study is to correlate tumour dimensions obtained by thresholds of standardized uptake value (SUV; static PET), metabolic rate of glucose (MRglu; dynamic PET) with pathological data. The most appropriate method may quicken tumour delineation for radiotherapy planning.

Material and Methods: Patients with curatively resected NSCLC were included in this prospective study (n=35). Dynamic 18FDG-PET scans were acquired during 60 minutes. Patlak analyses using the data acquired between 15-60 minutes post-injection were performed to calculate parametric images of MRglu. The last time frame was used as static PET scan. Tumour volumes were delineated using 50% of maximum, 40% of maximum above background and FLAB algorithm. Maximum SUV (SUVmax) and maximum MRglu (MRglu;max) were calculated. In on-going analysis, volumes acquired by the segmentation methods are correlated with pathology volumes to determine the optimal delineation method for NSCLC. Within the most appropriate method, pharmacokinetic rate constants k1, k2, k3, VB are currently being calculated using an irreversible two-compartment model.

Results: Initial results showed that SUVmax was higher in squamous cell NSCLCs versus adenocarcinomas (median 17.8 (9-33) versus 11.6 (6-32) respectively, p=0.002). Also the MRglu;max was higher in squamous cell carcinomas (median 462.6 nanomol/min/g (266.4-1366.2) versus 301.5 (129.7-1096.5) respectively, p=0.004).
Static volumes were larger compared to the dynamic volumes (p<0.001). Applying FLAB algorithm on static PET resulted in the largest volumes (p<0.001).

Conclusion: These preliminary data support differences in glucose metabolism between adeno- and squamous cell NSCLC. In the ongoing analyses, metabolic rates of glucose will be studied in more detail and will be correlated to survival. Furthermore, tumour volumes acquired by several segmentation methods will be correlated with pathology volumes to determine the optimal delineation method. This optimal segmentation method may aid in radiotherapy delineation.

EP-1852

Predictive role of FDG-PET/CT image-derived parameters in locally advanced oropharyngeal cancer

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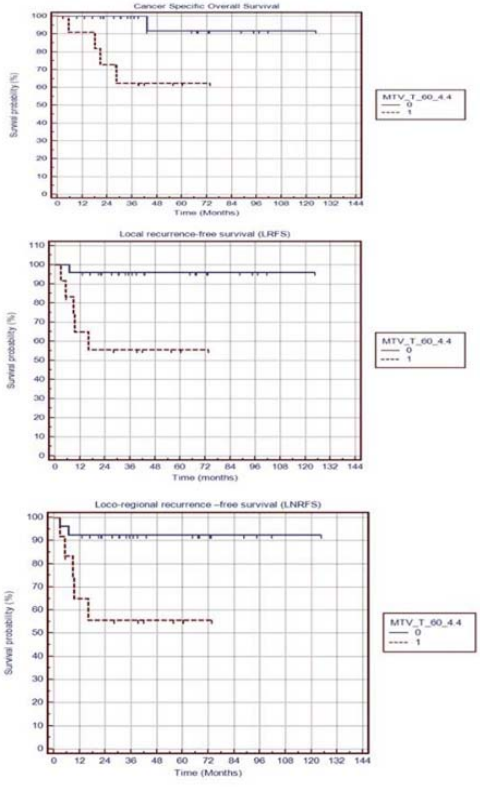
Purpose or Objective: To investigate the predictive role of FDG-PET/CT image-derived parameters in patients with locally advanced oropharyngeal cancer undergoing IMRT, by

means of helical tomotherapy (HTT), with a simultaneous integrated boost (SIB) on FDG-positive volumes (BTV).

Material and Methods: 41 patients (median age: 60; range: 41-81) treated between November 2005 and April 2014 at our Institution for advanced squamocellular oropharyngeal disease were analyzed. Most of the patients (95%) were of stage III-IV; 38 patients had positive lymph nodes (N, 32 with more than one N). HTT was delivered with a SIB approach in 30 fractions at different dose levels, concomitantly: 69 Gy (2.3 Gy/day) to FDG-positive volumes (primary tumor (T) and N), 66 Gy (2.2 Gy/day) to the tumor volume and enlarged nodes and 54 Gy (1.8 Gy/day) to the subclinical and elective treated nodes. PET metabolic parameters of FDG-positive volumes (T, N and T+N), including maximum and mean standardized uptake value (SUVmax and SUVmean), metabolic tumor volume (MTV) estimated at different thresholds 40-50-60% (MTV-40, MTV-50, MTV-60) and total lesion glycolysis (TLG-40, TLG-50, TLG-60) were considered. BTV volumes for T (BTV-T), N (BTV-N) and T+N (BTV-T+N) were also considered. Log rank univariate and Cox regression multivariate analysis were used to evaluate prognostic values of PET derived parameters and cancer specific overall survival (CSOS), local recurrence-free survival (LRFS) and loco-regional recurrence –free survival (LNRFS). The best cut-off values of PET derived parameters discriminating between patients with/without death/relapse were assessed by ROC analysis.

Results: The median follow-up was 37 months (range: 3-125 months). The 3-year CSOS, LRFS and LNRFS were 88.5%, 85% and 80%, respectively. At univariate analysis MTV-T-60>4.4cc was found the most significant PET parameter correlated to CSOS (HR: 0.09, p=0.0078), LRFS (HR: 0.07, p=0.0017) and LNRFS (HR: 0.16, p=0.01). TLG-T-60, SUVmean(T+N), MTV-T+N-60 were also found to be correlated with CSOS and LRFS. At multivariate analysis BTV-T+N>30.9cc and MTV-T-60>4.4cc were found the variables most significantly correlated with CSOS (AUC: 0.885; 95%CL: 0.739-0.965). MTV-T-60>4.4cc confirms its independent predictive role for LRFS (AUC: 0.807; 95%CL: 0.647-0.917) and for LNRFS (AUC: 0.744; 95%CL: 0.577-0.872).



CCOS, LRFS and LNRFS according to MTV_T_60>4.4cc and MTV_T_60≤ 4.4cc

Conclusion: FDG PET/CT performed as guide for HTT SIB treatment in patients affected by advanced oropharyngeal cancer is predictive of patient's outcome. MTV-T-60 was found the best predictor for CSOS, LRFS and LRNFS. FDG-PET/CT image-derived parameters might be useful to select more personalized treatment strategies.

EP-1853

Correlation between biomarkers derived from PET/CT and diffusion-weighted MRI in esophageal cancer

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Purpose or Objective: Both the standardized uptake value (SUV), acquired by 18F-flurodeaxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT), and the apparent diffusion coefficient (ADC) acquired by diffusion-weighted magnetic resonance imaging (DW-MR) are well established measures for treatment response assessment in neoadjuvant esophageal cancer treatment. However, these functional imaging parameters may refer to different aspects of tumor pathophysiology. Currently it is unclear whether these two prognostic biomarkers provide similar information or represent independent biomarkers. Therefore the aim of this study was to evaluate the correlation between SUV and ADC measurements in untreated esophageal tumors.

Material and Methods: This prospective study included 33 patients with histologically proven esophageal cancer who underwent 18F-FDG PET/CT and DW-MR examinations within 3 weeks before therapy. Tumor glucose metabolism was evaluated by the maximum and mean SUV (SUVmax and SUVmean) on the 18F-FDG PET/CT images. Minimum and mean ADC values (ADCmin and ADCmean, calculated with b values of 0,200 and 800 s/mm2) were measured in the same lesions. Lesions with a diameter larger than 3 cm were matched and a voxelwise analysis of ADC and SUV was performed. Spearman's rank correlation coefficients were used to assess the correlation between 18F-FDG PET and ADC metrics. Also the tumor ADCmean and SUVmax was compared between squamous cell carcinomas and adenocarcinomas, and between moderately and poorly differentiated tumors.

Results: Mean ADCmean and ADCmin of the 33 included esophageal cancer tumors were 1.8 ± 0.4 and 0.8 ± 0.4, *10-3mm2/s, respectively. Mean SUVmean and Mean SUVmax were 8.3 ± 4.2 and 17.4 ± 9.6, respectively. The SUV and ADC values as measures of glucose metabolism and cell density, respectively, showed weak to very weak non-significant correlations only (ADCmin vs SUVmax; r=0.30, p=0.09], [ADCmin vs. SUVmean r=0.30 p=0.09], [ADCmean vs SUVmax r=0.17 p=0.36], [ADCmean vs SUVmean r=0.14 p=0.43]) (Figure 1). The voxel-wise analysis of 16 esophageal tumors with diameters larger than 3 cm showed a weak but significant negative correlation between ADC and SUV in 11 patients. ADCmean was significantly related to histological tumor grade (2.0 ± 0.3 in moderately differentiated tumors vs. 1.6 *10-3mm2/s in poorly differentiated tumors (p=0.014)). No difference between squamous cell carcinoma and adenocarcinoma was found. SUVmax showed no differences with regard to tumor type and differentiation grade.